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Brain Scintigraphy and Intracranial Neoplasms

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SINCE BRAIN SCINTIGRAPHY was introduced more than 20 years ago it has become a well-established procedure in the diagnosis of neurological disorders. Its value in the diagnosis of intracranial neoplasms has been well-documented in several series carried out in large medical centers.[1-5] This report shows comparably good results in a 200 to 300 bed community hospital in a period of 11 years.

Methods and Materials

The case records of 73 patients in whom the diagnosis of brain tumors had been made were reviewed from the surgical and autopsy files for January 1964 through March 1975 in the Scripps Memorial Hospital. The cases of 69 patients in whom brain scintigrams were carried out within one month before surgical operation or autopsy were selected for the study. Two patients were excluded because the brain scintigrams were done 3 and 3½ months, respectively, before surgical operation. Two other patients were excluded because brain scans were not done until after operation. All patients except two were adults ranging from 19 to 70 years old. The two exceptions were an 11-year-old girl with dysgerminoma of the hypothalamus and a 12-year-old boy with Grade I astrocytoma of the left occipital area.

During the 11-year study period, a variety of radiopharmaceuticals and instruments were used. Of the 69 patients in the study, two patients received mercury-203 (Hg-203) chloromerodrin (750 microcuries) and five patients had mercury-197 (Hg-197) chloromerodrin (750 microcuries) in the early part of the study in 1964. These patients were scanned at 24 hours postinjection using a Nuclear-Chicago PhoDot scanner with 3 × 2 inch thallium activated sodium iodide crystal and a 19 hole collimator with a focal depth of 8 cm. The spectrometer was set at 260 to 300 kiloelectron volts (kev) for Hg-203 and 71 to 83 kev for Hg-197. Speeds for the scanner were 12 cm per minute for Hg-203 and 20 cm per minute for Hg-197 with a spacing of 4 mm. After 1964, technetium-99m (Tc-99m) in the form of pertechnetate or glucoheptonate was the radiopharmaceutical used for brain imaging. Sixty patients received 15 millicuries Tc-99m pertechnetate and the remaining two patients received 15 millicuries of Tc-99m glucoheptonate. Potassium perchlorate (800 mg) was given orally to the patients 15 minutes before the study in order to block the uptake by the choroid plexus, salivary gland and thyroid. Since the use of Tc-99m, the imaging instruments include a Searle Pho-Gamma III scintillation camera, a Searle Pho-Gamma III HP scintillation camera and a Nuclear Data Radicamera 60 scintillation camera. Cerebral flow studies were routinely carried out on the scintillation camera. High sensitivity collimators were used for the flow study with a 30 percent window while high resolution collimators were used for the static scintiphotos with a 20 percent window. Static scintiphotos with 350,000 counts were obtained at 1½ to 2 hours after injection of

TABLE 1.—*Sensitivity of Brain Scintigraphy by Tumor Size*

	No. of Cases	*Cases with Positive Scintigram*	*Sensitivity (percent)*
All cases	69	61	88.4
Larger than 2 cm	59	56	94.9
Equal to or less than 2 cm	10	5	50.0

TABLE 2.—*Sensitivity of Brain Scintigraphy by Location of Tumor*

	No. of Cases	*Cases with Positive Scintigram*	*Sensitivity (percent)*
All cases	69	61	88.4
Cerebrum	56	53	94.6
Pituitary fossa	4	2	50.0
Posterior fossa	9	6	66.7

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pertechnetate and ½ hour after glucoheptonate. All scintigrams were obtained in the anterior, posterior and both lateral positions. If necessary, delayed scintigrams were obtained at four to six hours postinjection.

Results

The brain scintigrams were abnormal in 61 of 69 patients, representing an overall sensitivity of 88.4 percent in our study.

The size and location of the tumors are the main factors affecting their detectability. For example, tumors of 2 cm or less in diameter were not diagnosed in 5 of 10 cases (50 percent) whereas only 3 of 59 cases (5.1 percent) of tumors greater than 2 cm in diameter were missed (Table 1). Deep seated tumors around the pituitary fossa are more difficult to detect by brain scan and two of four cases were not detected in our study (Table 2). A total of 26 metastatic intracranial neoplasms was present in our study. Two of four metastatic tumors in the cerebellum were missed and both of them were less than 2 cm in diameter. However, only one of 22 metastatic tumors in the cerebrum was not correctly diagnosed. The primary sites of the metastatic tumors were by majority the lung (15), followed by the breast (1), kidney (1), nasopharynx (1), melanoma (1), ovary (1), reticulum cell sarcoma (1) and lesions of unknown origin (5). The histological types of tumor and their overall detectability are summarized in Table 3. All high grade astrocytomas were diagnosed correctly whereas one of four low grade astrocytomas was missed. All gliomas of the cerebellum were correctly diagnosed whereas one of two acoustic neurilemmomas of 1.3 cm in diameter gave false negative findings on the brain scintigram. The single cases of colloid cyst, craniopharyngioma and cystic ependymoma all gave false negative results.

TABLE 3.—*Results of Brain Scans According to Histological Types*

Location and Histologic Type	*No. of Cases*	*Scan Findings*	
		Negative	*Positive*
Cerebrum			
Astrocytoma			
Grade I-II	4	1	3
Grade III-IV	16	0	16
Oligodendroglioma	1	0	1
Mixed glioma	1	0	1
Meningioma	9	0	9
Metastatic tumors	22	1	21
Ependymoma (cystic)	1	1	0
Undifferentiated tumor	2	0	2
Cerebellum			
Acoustic neurilemmoma	2	1	1
Metastatic tumor	4	2	2
Glioma	3	0	3
Pituitary fossa			
Chromophobe adenoma	1	0	1
Dysgerminoma	1	0	1
Craniopharyngioma	1	1	0
Colloid cyst	1	1	0

TABLE 4.—*Accuracy of Brain Scan in Proven Intracranial Tumors*

Authors	*Total No. of Cases*	*Cases with Positive Brain Scintigram*	*Sensitivity (percent)*
Goodrich et al (1965)	118	99	84.0
Overton et al (1965)	100	84	84.0
Witcofski et al (1967)	92	75	81.5
O'Mara and Mozley (1971)	88	73	83.0
Authors	69	61	88.4

Discussion

With the currently available instruments, our results in brain scintigraphy compare favorably with reports from large medical centers (Table 4). Our results indicate that size and location are important factors affecting the detection of brain tumors. Boller and co-authors[6] showed that brain tumors larger than 2.7 cm in diameter were missed by scintigraphy in only 3 percent of cases. As is the experience of others, we had very good results with high grade astrocytomas, supratentorial meningiomas and metastatic tumors in the cerebrum. Midline tumors around the pituitary fossa or lesions of 2 cm or less in diameter are not easily detected by the Anger scintillation camera. Tomographic data obtained with a rectilinear scanner or, better still, with a multiplane

TABLE 5.—*Neurodiagnostic Tests and Their Relative Percent Accuracy*

Authors	*Brain Scan*	*Skull Series*	*Echoencephalogram*	*Electroencephalogram*	*Arteriogram*	*Pneumoencephalogram and Ventriculography*
Goodrich et al	84.0	40.0	..	92.0	82.0	84.0
Overton et al	84.0	37.0	..	71.0	84.0	95.0
Witcofski et al	81.5	46.9	68.9	70.4	92.3	93.9
O'Mara and Mozley	83.0	..	..	..	86.5	95.4

tomographic scanner[7] may be expected with proper positioning to yield better results with midline tumors. Newer radiopharmaceuticals such as Tc-99m glucoheptonate and Tc-99m diethylenetriaminepentacetic acid (DTPA) are cleared rapidly from the blood stream and show little free pertechnetate concentration in mucosal areas. They would tend to improve the ability to detect abnormal concentrations of tracer near the base of the brain, particularly in the midline and in the posterior fossa.

The timing of brain scintigraphy after injection also affects the sensitivity of the procedure. Generally, delayed scintigraphy at three to four hours after injection of Tc-99m pertechnetate gives better results than early scans done within one hour after injection. Gates and co-authors[8] improved the detectability of brain tumors from 80 percent with routine early scintigraphy to 93 percent with delayed studies. Ramsey and Quinn[9] also confirmed the presence of increased visible abnormality in the delayed scintigrams in 39 of 74 patients with proven intracranial disease. Meisel and co-authors[10] suggest the use of delayed scintigraphy with 203 Hg-chlormerodrin at 24 hours after injection when delayed Tc-99m pertechnetate scintigrams are negative or equivocal in patients suspected of having lesions adjacent to the base of the skull, especially in the subtentorial region.

The greatest advantage of brain scintigraphy is its noninvasiveness. The overall accuracy of brain scintigraphy is about the same as cerebral arteriography,[4,11-13] which carries a significantly higher risk to the patient. Table 5 shows a comparison of the percent diagnostic accuracy of different neurodiagnostic tests. Unlike echogram or electroencephalogram, brain scan permits accurate and direct localization and visualization of the tumor, which is important to the neurosurgeon. The higher accuracy of pneumoencephalogram and ventriculography may represent an additive effect due to the use of brain scintigraphy as a screening test before performance of the air studies.[4] The successfulness of different procedures in brain tumor detection also depends on their location. While brain scintigraphy is very good in detecting superficial lesions, air contrast studies are better in deep-seated midline tumors.

The use of brain scintigraphy should not be considered as a competition to other radiological procedures but rather as a complement. For example Witcofski and co-authors[3] used brain scintigraphy to select the appropriate x-ray contrast study to improve the final diagnostic accuracy. While arteriography provides more precise information of the vascularization of the tumor, the direct visualization of lesions on the brain scintigram is often superior to the indirect evidence of displacement of vascular structures or air-filled spaces as in x-ray contrast studies.[4]

For the past 20 years brain scintigraphy has proved to be a useful tool in screening intracranial neoplasms. Newly available methods will, however, permit even a higher successful rate in the detection of brain tumors in the near future. Ostertag and co-authors[14] applied a dual isotope technique with scintigraphic and orthagonal multiple field digital measurements and succeeded in detecting more than 90 percent of basal supratentorial midline cerebral tumors and posterior fossa tumors. Kuhl and associates have developed a method of reconstructing a transaxial tomographic section of the head from a series of rectilinear scans carried out with scintillation detectors of conventional design.[15-17] Computerized axial tomography (CAT) with the EMI® scanner[18] (manufactured by EMI Medical, Inc., 3605 Woodhead Drive, Northbrook, IL 60062) is a revolutionary radiographic scanning technique that takes multiple x-ray transmission readings through the skull at one degree increments around the head. The linear x-ray attenuation coefficients of the brain tissues and cerebrospinal fluid are calculated on a computer and displayed pictorially as axial transverse layers of the head. Initial clinical trials[19-26] suggest that CAT provides a potentially powerful tool for the detection of intracranial neoplasms. The exact impact of CAT on radionuclide brain scintigraphy is still uncertain at present; however, the two procedures will likely be complementary to one another and in patients who cannot lie still or who are sensitive to iodinated contrast media, radionuclide brain scintigraphy would remain the procedure of choice.

The radiation dose from 15 millicuries of Tc-99m pertechnetate is approximately 0.16 rad to the whole body and 3 rads to the colon.[27] The small radiation dose permits brain scintigrams to be done in all age groups and to be repeated if necessary. Serial brain scintigrams are useful to assess the efficacy of various forms of therapy.

Summary

The diagnostic accuracy of brain scintigraphy in 69 histologically proven brain tumors was

studied in a 200 to 300 bed community hospital. The overall detectability of 88.4 percent favorably compares with results of several series carried out in large medical centers. The noninvasiveness and overall accuracy of brain imaging renders it a reliable procedure for screening patients with suspected intracranial neoplasms.

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Problems of Females Exposed to DES *In Utero*

Those female infants born to mothers who have received DES (diethylstilbestrol) are found to have a substantial probability of abnormalities of the cervix and vagina. I am cautious to say "abnormalities" of the cervix and vagina because they have *not* been found to have a very great likelihood of developing cancer. Indeed, in some large series of screening of patients whose mothers received DES, no case of vaginal or cervical cancer has been found. What has been found are lesions of the vagina and cervix which we call adenosis. On the other end of the scale, a very few patients have been seen with carcinoma of the vagina or cervix (clear-cell type). Essentially, all of these cases were products of a pregnancy that was exposed to DES. But that is not to say that many of the children who were so exposed will develop cancer, because most of them will not. It is important to explain that to the patient and to her parents. Her degree of risk of developing cancer is exceedingly slight, but it does exist.

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